

## (12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau



(43) International Publication Date  
19 February 2004 (19.02.2004)

PCT

(10) International Publication Number  
**WO 2004/014419 A1**

(51) International Patent Classification<sup>7</sup>: **A61K 39/095, 39/102, 39/00**

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(21) International Application Number:  
**PCT/EP2003/008567**

(22) International Filing Date: 31 July 2003 (31.07.2003)

(25) Filing Language: English

(26) Publication Language: English

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(30) Priority Data:

0218037.0	2 August 2002 (02.08.2002)	GB
0218036.2	2 August 2002 (02.08.2002)	GB
0218035.4	2 August 2002 (02.08.2002)	GB
0218051.1	2 August 2002 (02.08.2002)	GB
0220197.8	30 August 2002 (30.08.2002)	GB
0220199.4	30 August 2002 (30.08.2002)	GB
0225524.8	1 November 2002 (01.11.2002)	GB
0225531.3	1 November 2002 (01.11.2002)	GB
0230164.6	24 December 2002 (24.12.2002)	GB
0230168.7	24 December 2002 (24.12.2002)	GB
0230170.3	24 December 2002 (24.12.2002)	GB
0305028.3	5 March 2003 (05.03.2003)	GB

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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**Published:**

- *with international search report*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

WO 2004/014419 A1

(54) Title: VACCINE COMPOSITION COMPRISING TRANSFERRIN BINDING PROTEIN AND HSF FROM GRAM NEGATIVE BACTERIA

(57) Abstract: The present invention relates to immunogenic compositions and vaccines for the prevention or treatment of Gram negative bacterial infection. Immunogenic compositions of the invention comprise transferrin binding protein and Hsf, and the combination of these two antigens have been shown to act synergistically to produce antibodies with high activity in a serum bactericidal assay. This combination of antigens is useful for use in vaccines against *Neisseria meningitidis*, *Neisseria gonorrhoeae*, *Moraxella catarrhalis* and *Haemophilus influenzae*.

# INTERNATIONAL SEARCH REPORT

Intern. Application No  
PCT/EP 03/08567

**A. CLASSIFICATION OF SUBJECT MATTER**  
**IPC 7 A61K39/095 A61K39/102 A61K39/00**

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
**IPC 7 A61K**

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

**EPO-Internal, WPI Data, EMBASE, BIOSIS, MEDLINE**

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 01 09350 A (DALEMANS WILFRIED L J ;SMITHKLINE BEECHAM BIOLOG (BE); THIRY GEORG) 8 February 2001 (2001-02-08)            cited in the application            abstract            page 12, line 32 -page 13, line 14            page 14, line 12 - line 22            page 20, line 11 - line 22            page 23, line 21 -page 24, line 7            page 25, line 11 -page 27, line 22            page 31, line 1 - line 22            page 31, line 30 -page 32            page 33, line 12 - line 30            page 36, line 11 - line 19            example 8            ---            -/-</p>	20-25, 27-45, 51-63,65

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

**9 January 2004**

Date of mailing of the international search report

**20/01/2004**

Name and mailing address of the ISA

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## INTERNATIONAL SEARCH REPORT

Internl	Application No
PCT/EP 03/08567	

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 00 71725 A (PIZZA MARIAGRAZIA ;RAPPUOLI RINO (IT); CHIRON SPA (IT); GIULIANI M) 30 November 2000 (2000-11-30) cited in the application  abstract page 55, line 1-3 ---	1-8,13, 14, 16-19, 48-51, 55-59, 61,65
A	WO 00 25811 A (GORRINGE ANDREW RICHARD ;HUDSON MICHAEL JOHN (GB); MICROBIOLOGICAL) 11 May 2000 (2000-05-11) cited in the application abstract page 1, paragraph 1 page 3, last paragraph -page 4, paragraph 1 page 5, paragraph 4 -page 6, paragraph 1 page 6, paragraph 3 page 7, paragraph 5 -page 8, paragraph 1 claims 1,10-16,27,32 ---	
A	WO 99 31132 A (JENNINGS MICHAEL PAUL ;PEAK IAN RICHARD ANSELM (AU); UNIV QUEENSLA) 24 June 1999 (1999-06-24) cited in the application abstract page 34, line 10 -page 40, line 17 claims 1-11,20,21,29-33 ---	1-19, 48-52, 55-59, 66-71
A	WO 01 72337 A (GORRINGE ANDREW RICHARD ;HUDSON MICHAEL JOHN (GB); MICROBIOLOGICAL) 4 October 2001 (2001-10-04)  abstract page 5, line 14 - line 26 page 7, line 21 -page 8, line 10 page 10, line 6 - line 37 ---	1-3, 5-10,13, 14, 16-19, 46,47,64
A	MATHERS K ET AL: "ANTIBODY RESPONSE TO OUTER MEMBRANE PROTEINS OF MORAXELLA CATARRHALIS IN CHILDREN WITH OTITIS MEDIA" PEDIATRIC INFECTIOUS DISEASE JOURNAL, WILLIAMS & WILKINS, BALTIMORE, MD, US, vol. 18, no. 11, November 1999 (1999-11), pages 982-988, XP009003591 ISSN: 0891-3668 abstract -----	

## INTERNATIONAL SEARCH REPORT

Int'l application No.  
PCT/EP 03/08567

### Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:  
**Although claims 56,57,70 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.**
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
**see FURTHER INFORMATION sheet PCT/ISA/210**
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

#### Remark on Protest

- The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

International Application No. PCT/EP 03 08567

### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

#### Continuation of Box I.2

Present claims 1,20,21,26-32,35-43,45-48,51-56,58,60 relate to an extremely large number of possible immunogenic compositions and bacterial strains. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the immunogenic compositions and bacterial strains claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the immunogenic compositions comprising proteins or outer membrane vesicles derived from *Neisseria*, *Moraxella catarrhalis* and *Haemophilus influenzae* (see examples and description page 12, last paragraph -page 14, paragraph 2).

Present claims 1-14, 16,18,20-43,45-48,51-71 relate to compounds defined by reference to a desirable characteristic or property, namely being a Hsf like protein or as defined in the description on page 9, line 3-4, sharing homology with Hsf of *Neisseria meningitidis*. The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds disclosed in the description on page 9, line 11-25.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

## INTERNATIONAL SEARCH REPORT

Information on patent family members

Intern

Application No

PCT/EP 03/08567

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